BINDING OF β-AMYLOID TO C1q AND CELLULAR SUSCEPTIBILITY TO COMPLEMENT ACTIVATION

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Recent in vitro studies have shown that β-amyloid (βA) binds to C1q and can activate the complement cascade.

In the present study we determined whether the state of aggregation of βA peptides affects their binding to C1q and examined whether the susceptibility of PC12 cells and of hippocampal neurons to βA peptides is aggravated in the presence of complement. Freshly dissolved [^{125}I]βA(1-40) and [^{125}I]βA(1-28) bind to C1q in similar and biphasic curves. The first phase exhibits saturation characteristics with K_D ~ 4μM and a 1:1 stoichiometry. The second phase of the binding curve has a lower affinity and a higher capacity and does not saturate at peptide levels up to at least 70 μM. Aging of the peptides by preincubation at 37°C for 24 h markedly reduces the binding of [^{125}I]βA(1-40) to C1q but has no effect on the binding of [^{125}I]βA(1-28) to C1q. Tissue culture neurotoxicity experiments revealed that βA(1-40) and βA(25-35) reduce cellualr viability. However, complement had no additive effect on the cytotoxicity of these peptides. Furthermore, βA(1-28) which binds to C1q and is by itself not toxic, was also not toxic when added to the cultures in the presence of complement. The implications of these findings regarding the possible involvement of βA mediated complement activation in Alzhimer's disease are discussed.

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